

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of
TERRELL, Ross C.

Serial No. 07/010,106

Filed: February 2, 1987

For: ANESTHETIC COMPOSITION AND
METHOD OF USING THE SAME

Group Art Unit: 125

Examiner: J. Goldberg

Atty. Dkt.: PP4351

Date: January 22, 1988

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

DECLARATION UNDER RULE 132

Sir:

I, Gerald G. Vernice, hereby declare and say as
follows:

I received an B.S. Degree in Chemistry from St.
Peter's College and an M.S. Degree in chemistry from Fairleigh
Dickinson University.

I am the author or co-author of 12 scientific
publications and patents. I am a member of the Parenteral Drug
Association, The American Chemical Society, The New York
Academy of Science, The American Association for the
Advancement of Science and The International Society of
Pharmaceutical Engineers.

I am currently, Group Leader Chemistry for Anaquest
Division of BOC, Inc., the assignee of the above-identified
patent application S.N. 07/010,106, filed on February 2, 1987
for an Anesthetic Composition and Method of Using the Same.

I have 24 years experience in the pharmaceutical
industry.

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I am familiar with the invention disclosed and claimed in the above-identified patent application.

I am familiar with the prosecution of said application in the United States Patent Office and the prior art cited in the course of the prosecution;

I currently chair Anaquest's Research Review Committee for New Inhalation Anesthetics.

I declare that for measurement of the efficacy of a potential new volatile general anesthetic there must be an objective end point which correlates well with "anesthesia". The loss of the righting reflex is a criteria which has served well in a large number of animal studies. In addition to being easily observed it has the advantage of being a quantal response.

I declare that to the best of my knowledge experiments (animal trials) according to the following Experimental Procedure were conducted at the University of Maryland under contract to Anaquest and that to the best of my knowledge the results shown in Table I summarizes the results of the experiments.

Experimental Procedure: The technique chosen for the study of loss of righting was that of Cascorbi and Rudo, Anes. and Analg. 43:163-167 (1964). Swiss Webster male mice, ideally between 20 and 25 grams, were used. A wide mouth screw top vessel of 3-4 liter volume was flushed with oxygen and a calculated amount of the test agent was introduced (the initial test concentration was 2.5%). The jar was closed and agitated to ensure complete vaporization. A number of mice were poured into the jar, which was placed on a rack and rotated about every 30 seconds to note loss of righting. The nature of the observations made were flexible. If the anesthetic is potent

or the concentration high, it will suffice to measure the time to loss of righting (which may be 30 seconds or less).

After the period of anesthetic exposure (a maximum of 10 minutes regardless of whether anesthesia is achieved) the mice were poured onto the bench and the time to recovery of the righting reflex was then measured.

Induction time is the time in seconds from closure of the jar to loss of righting, and is recorded for each mouse. The average value is used in a summary sheet. Recovery time is the time in seconds after removal from the jar to the moment when an animal is able to walk.

Table I shows a comparison of the two agents, $\text{CHF}_2\text{OCHFCF}_3$ (according to the claimed method of use) and the bromo analog $\text{CHF}_2\text{OCHBrCF}_3$, at the highest concentration the anesthetic is at an approximately equipotent concentration which allows a comparison of the pharmacologic properties of said agents. Thus at 2.5%, the bromo analog is equipotent to 10% of the fluoro compound.

TABLE I

<u>Structure</u>	<u>Dose</u>	<u>Induction (sec)</u>	<u>Recovery (sec)</u>
$\text{CHF}_2\text{-O-CHBrCF}_3$	0.5%	280	26
	1%	58	100
	1.5%	27	186
	2.5%	20	449
$\text{CHF}_2\text{-O-CHFCF}_3$	5%	50 light	5
	10%	15	25

Based on my review of the available data, the inhalation anesthetic $\text{CHF}_2\text{-O-CHFCF}_3$ exhibits substantially faster recovery than $\text{CHF}_2\text{-O-CHBrCF}_3$.

I declare further that all statements made in this declaration of my own knowledge are true and that all statements made on information and belief are believed to be

true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

1-22-88

Date

Gerald G. Vernice

Gerald G. Vernice - GIK